Sector 3
Box SEQ

PATENTS #5

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

David N. COOPER et al.

Serial No. 09/853,688 GROUP 1623

Filed May 14, 2001

METHOD FOR DETECTING GROWTH HORMONE VARIATIONS IN HUMANS, THE VARIATIONS AND THEIR USES

AMENDMENT

Commissioner for Patents

Washington, D.C. 20231

Sir:

Prior to examination on the merits, please amend the above-identified application as follows:

IN THE SPECIFICATION:

Replace the paragraph beginning at page 22, line 27 with the following rewritten paragraph:

--CTC CGC GTT CAG GTT GGC (GHD1F) (SEQ ID NO: 12);

AGG TGA GCT GTC CAC AGG (GHD1R) (SEQ ID NO: 13);

CTT CCA GGG ACC AGG AGC (GHD2R) (SEQ ID NO: 14);

CAT GTA AGC CAA GTA TTT GGC C (GHD3F) (SEQ ID NO: 15);

GGA GAA GGC ATC CAC TCA CGG (GHD4R) (SEQ ID NO: 16);

TCA GAG TCT ATT CCG ACA CCC (GHD5F) (SEQ ID NO: 17);

CGT AGT TCT TGA GTA GTG CGT CAT CG (GHD6R) (SEQ ID NO: 18); and

TTC AAG CAG ACC TAC AGC AAG TTC G (GHD7F) (SEQ ID NO: 19);--.

GH1G3 (5' CTCGAGCTAGAAGCCACAGCTGCCC 3') (SEQ ID NO: 31)--.

Replace the paragraph beginning at page 46, line 8, with the following rewritten paragraph:

--BGH3 (5' TAGAAGGCACAGTCGAGG 3') (SEQ ID NO: 59)--.

Replace the paragraph beginning at page 46, line 20, with the following rewritten paragraph:

--GH1R5 (5' ATGGCTACAGGCTCCCGG 3') (SEQ ID NO: 60); and

GH1R3 (5' CTAGAAGCCACAGCTGCCC 3') (SEQ ID NO: 61)--.

IN THE DRAWINGS:

Permission is respectfully requested to amend the drawings as marked in red on the attached sheet.

Please make of record the attached paper and disk versions of a Sequence Listing.

Charge the late filing fee oath or declaration surcharge of $130 to Deposit Account No. 25-0120.

REMARKS

The Notice to File Missing Parts mailed August 29, 2001 called for submission of an executed declaration, substitute drawings, and a Sequence Listing. All three of those elements

Replace the paragraphs beginning at page 23, line 5 through line 17 with the following rewritten paragraphs:

--GTGCCCCAAGCCTTTCCC (LCR15: 1159-1177) (SEQ ID NO: 20);

TGTCAGATGTTCAGTTCATGG (LCR13: 1391-1412) (SEQ ID NO: 21);

CCTCAAGCTGACCTCAGG (LCR25: 1346-1363) (SEQ ID NO: 22); and

GATCTTGGCCTAGGCCTCG (LCR23: 1584-1602) (SEQ ID NO: 23); and also

LCR 5A (5′ CCAAGTACCTCAGATGCAAGG 3′) (SEQ ID NO: 24); and

LCR 3.0 (5′ CCTTAGATCTTGGCCTAGGCC 3′) (SEQ ID NO: 25); and also

LCR 5.0 (5′ CCTGTCACCTGAGGATGGG 3′) (SEQ ID NO: 26);

LCR 3.1 (5′ TGTGTTGCCTGGACCCTG 3′) (SEQ ID NO: 27);

LCR 3.2 (5′ CAGGAGGCCTCACAAGCC 3′) (SEQ ID NO: 28); and

LCR 3.3 (5′ ATGCATCAGGGCAATCGC 3′) (SEQ ID NO: 29) are suitable for sequencing the 1.9kb fragment.--

Replace the paragraphs beginning at page 23, line 22 through line 27 with the following rewritten paragraphs:

--GH1G5 (5' GGTACCATGGCTACAGGTAAGCGCC 3') (SEQ ID NO: 30);

GH1G3 (5' CTCGAGCTAGAAGCCACAGCTGCCC 3') (SEQ ID NO: 31);

BGH3 (5' TAGAAGGCACAGTCGAGG 3') (SEQ ID NO: 32);

GH1R5 (5' ATGGCTACAGGCTCCCGG 3') (SEQ ID NO: 33); and

GH1R3 (5' CTAGAAGCCACAGCTGCCC 3') (SEQ ID NO: 34).--

Replace the paragraph beginning at page 36, line 10, with the following rewritten paragraph:

--Oligonucleotide primers GH1F (5′ GGGAGCCCCAGCAATGC 3′(SEQ ID NO: 35); -615 to -599) and GH1R (5′ TGTAGGAAGTCTGGGGTGC 3′(SEQ ID NO: 36); +2598 to +2616) were designed to correspond to *GH1*-specific sequences in order to PCR amplify a 3.2kb single genomic DNA fragment containing the human *GH1* gene using the Expand™ high fidelity system (Roche).--

Replace the heading beginning at page 39, line 1, with the following rewritten heading:

--Table 6 Oligonucleotide primers used for DHPLC analysis and DNA sequencing (SEQ ID NOS: 37-50, respectively)--.

Replace the paragraph beginning at page 40, line 25, with the following rewritten paragraph:

--GH1S1 (5′ GTGGTCAGTGTTGGAACTGC 3′(SEQ ID NO: 51): -556 to -537);
GH3DF (5′ CATGTAAGCCAAGTATTTGGCC 3′(SEQ ID NO: 52): +189 to +210);
GH4DF (5′ GACTTTCCCCCGCTGTAAATAAG 3′(SEQ ID NO: 53): +541 to +560): and
GH6DF (5′ TCCCCAATCCTGGAGCCCCACTGA 3′(SEQ ID NO: 54): +1099 to +1122).--

Replace the paragraph beginning at page 41, line 29, with the following rewritten paragraph:

--Fragment 1 primers were LCR15 (5′ GTGCCCCAAGCCTTTCCC 3′: 1159-1177) (SEQ ID NO: 55) and
LCR13 (5′ TGTCAGATGTTCAGTTCATGG 3′: 1391-1412) (SEQ ID NO: 56); and
fragment 2 primers were LCR25 (5′ CCTCAAGCTGACCTCAGG 3′(SEQ ID NO: 57): 1346-1363) and LCR23 (5′ GATCTTGGCCTAGGCCTCG 3′(SEQ ID NO: 58): 1584-1602).--

Replace the paragraph beginning at page 42, line 22, with the following rewritten paragraph:

--LCR 5A (5′ CCAAGTACCTCAGATGCAAGG 3′) (SEQ ID NO: 24); and
LCR 3.0 (5′ CCTTAGATCTTGGCCTAGGCC 3′(SEQ ID NO: 25); see Figure 4),--.

Replace the paragraph beginning at page 43, line 1, with the following rewritten paragraph:

--LCR 5.0 (5′ CCTGTCACCTGAGGATGGG 3′) (SEQ ID NO: 26);
LCR 3.1 (5′ TGTGTTGCCTGGACCCTG 3′) (SEQ ID NO: 27);
LCR 3.2 (5′ CAGGAGGCCTCACAAGCC 3′) (SEQ ID NO: 28); and
LCR 3.3 (5′ ATGCATCAGGGCAATCGC 3′) (SEQ ID NO: 29) were used to span the region.--

Replace the paragraph beginning at page 45, line 22, with the following rewritten paragraph:

--GH1G5 (5' GGTACCATGGCTACAGGTAAGCGCC 3') (SEQ ID NO: 30); and

GH1G3 (5' CTCGAGCTAGAAGCCACAGCTGCCC 3') (SEQ ID NO: 31)--.

Replace the paragraph beginning at page 46, line 8, with the following rewritten paragraph:

--BGH3 (5' TAGAAGGCACAGTCGAGG 3') (SEQ ID NO: 59)--.

Replace the paragraph beginning at page 46, line 20, with the following rewritten paragraph:

--GH1R5 (5' ATGGCTACAGGCTCCCGG 3') (SEQ ID NO: 60); and

GH1R3 (5' CTAGAAGCCACAGCTGCCC 3') (SEQ ID NO: 61)--.

IN THE DRAWINGS:

Permission is respectfully requested to amend the drawings as marked in red on the attached sheet.

Please make of record the attached paper and disk versions of a Sequence Listing.

Charge the late filing fee oath or declaration surcharge of $130 to Deposit Account No. 25-0120.

REMARKS

The Notice to File Missing Parts mailed August 29, 2001 called for submission of an executed declaration, substitute drawings, and a Sequence Listing. All three of those elements

are submitted herewith.

As to the Sequence Listing, applicants hereby state that the content of the attached paper and disk versions is the same, and that these introduce no new matter into the present application.

The present amendment to the specification introduces the 66 sequence identifier numbers at appropriate places throughout the specification, per the sequence rule requirements.

It is believed that this application is now in condition for examination on the merits, and the same is respectfully requested.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Respectfully submitted,

YOUNG & THOMPSON

By 

Andrew J. Patch
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Arlington, VA 22202
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October 29, 2001

Version with markings to show changes made

In the specification:

Paragraph beginning at line 27 of page 22 has been amended as follows:

CTC CGC GTT CAG GTT GGC (GHD1F) (SEQ ID NO: 12);

AGG TGA GCT GTC CAC AGG (GHD1R) (SEQ ID NO: 13);

CTT CCA GGG ACC AGG AGC (GHD2R) (SEQ ID NO: 14);

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TTC AAG CAG ACC TAC AGC AAG TTC G (GHD7F) (SEQ ID NO: 19);

Paragraphs beginning at line 5, page 23 through line 17 have been amended as follows:

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GATCTTGGCCTAGGCCTCG (LCR23: 1584-1602) (SEQ ID NO: 23); and also

LCR 5A (5′ CCAAGTACCTCAGATGCAAGG 3′) (SEQ ID NO: 24); and

LCR 3.0 (5′ CCTTAGATCTTGGCCTAGGCC 3′) (SEQ ID NO: 25); and also

LCR 5.0 (5′ CCTGTCACCTGAGGATGGG 3′) (SEQ ID NO: 26);

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Paragraph beginning at line 22 of page 42 has been amended as follows:

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Paragraph beginning at line 8 of page 46 has been amended as follows:

BGH3 (5' TAGAAGGCACAGTCGAGG 3') (SEQ ID NO: 59)

Paragraph beginning at line 20 of page 46 has been amended as follows:

GH1R5 (5' ATGGCTACAGGCTCCCGG 3') (SEQ ID NO: 60); and

GH1R3 (5' CTAGAAGCCACAGCTGCCC 3') (SEQ ID NO: 61)

Figure 3

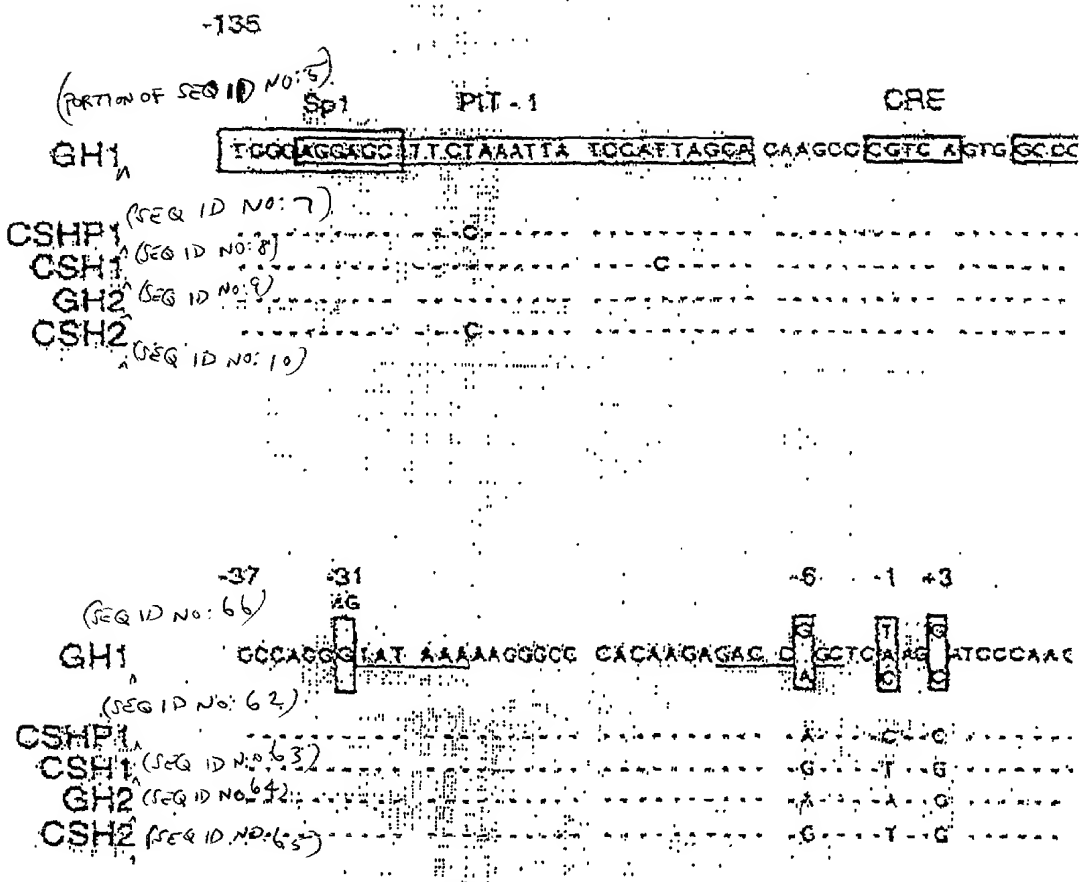

Fig. 3 Structure of the 5' untranslated region and promoter region of the human *GH1* gene. *Horizontal boxes* denote known, putative or inferred binding sites for transcription factors. *Vertical boxes* indicate polymorphic sites in the human population (data from Giordano et al. 1997; Wagner et al. 1997). The numbering scheme is by reference to the transcriptional initiation site at +1. The TATA box, a Chi-like element and the ATG translational initiation site are *underlined*. The human *GH1* promoter is also aligned with the promoters of the human *CSHP1*, *CSH1*, *GH2* and *CSH2* genes in order to indicate both the extent of homology but also the differences evident between promoters